distinctly claim the subject matter which applicant regards as the invention. Independent claims 35 and 42 have been amended as suggested by the Examiner. The amendment obviates this rejection.

II. Rejection under 35 U.S.C. §103, as being unpatentable over the prior art. Claims 35-51 have been rejected under 35 U.S.C. §103, as being unpatentable over Bachovchin (*J. Biol. Chem.* 265:3738-3743, 1990) or Bachovchin *et al.* (U.S. Patent 4,935,493) or Bachovchin *et al.* (WO 89/03223) or Flentke (*Proc. Natl. Acad. Sci. U.S.A.* 88:1556, 1991).

The Examiner cites a single statement in the *J. Biol. Chem.* Bachovchin reference (Bachovchin JBC) as grounds for rejecting the pending claims. Specifically, the Examiner takes the position that the statement "the early fraction appears, from the NMR spectra, to be approximately 95% enriched in one isomer" represents the description of a composition containing 95% of one isomer of a relevant compound.

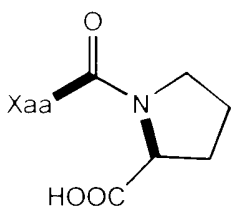
Applicant has previously pointed out that the statement made in Bachovchin JBC and relied upon by the Examiner *was an incorrect statement*, as has since been demonstrated in the literature and in declaratory evidence submitted to the Patent and Trademark Office (a copy of the previously submitted Declaration is enclosed with the present Response). The procedures followed in the Bachovchin JBC reference *did not*, and *can not*, produce a composition comprising 95% of one isomer of the compound. Thus, as Applicant has previously argued, the Bachovchin JBC reference does not teach one of ordinary skill in the art to produce a composition comprising 95% of one isomer, does not in fact describe such a composition, and therefore is not an enabling reference against the present claims. Applicant strongly reasserts this view.

In the Advisory Action mailed February 1, 2000, the Examiner has rejected Applicant's previous arguments with rationale that suggests a misunderstanding or misapplication of the law and the facts regarding the claimed invention. Specifically, the Examiner states "if a chemist stumbles onto the truth fortuitously, and reports in a publication that he obtained compound "X", such a report can be sufficient to bar a later scientist from being granted a monopoly on compound "X" even if the level of sophistication of the experiments carried out by the later

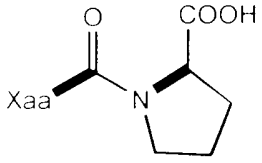
Bachovchin JBC *did not* stumble on the claimed composition: the authors did misidentify the resulting compounds as the ones claimed. The Examiner's position appears to be an inherency rejection – that the presently claimed invention is inherent in what Bachovchin JBC discloses. However, a proper inherency rejection requires that the reference be enabling and be reproducible. As is stated in **In re Wiggins**, 488 F.2d 538, 179 USPQ 421 (CCPA 1983), "the mere naming of a compound in a reference, without more, cannot constitute a description of the compound, particularly when, as in this case, the evidence of record suggests that a method suitable for its preparation was not developed until a date later than that of the reference." As amply described in the Declaration of April 1, 1999 and reiterated and amplified in the Declaration filed with this Response and discussed below, performing steps of Bachovchin JBC *does not* produce the stated result (*i.e.*, a composition containing 95% of one isomer).

The Examiner has previously challenged the assertions presented in the Bachovchin Declaration of April 1, 1999, but a careful analysis of the Examiner's comments reveals that they reflect a misunderstanding of the relevant technology. Specifically, in the Final Office Action mailed June 24, 1999, the Examiner offered a variety of technological reasons to reject the statements made in the April 1, 1999 Bachovchin Declaration. Many of the assertions made by the Examiner are scientifically inaccurate. Specific assertions are addressed individually below; a Table is also provided that summarizes Applicant's rebuttal of each of the Examiner's statements. A second Bachovchin Declaration is also provided, to support Applicant's rebuttal statements.

By way of background, Applicant first points out that, due to the partial double-bond character of the C-N linkage in an amide bond, certain amino acids, including proline, can exist in either a *cis* or a *trans* conformation with respect to the amide bond:

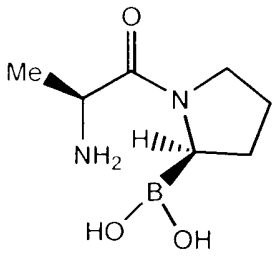


cis-Pro

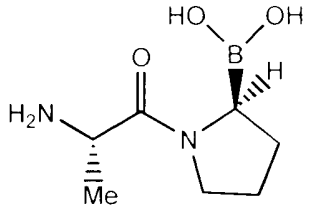


trans-Pro

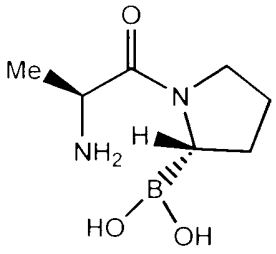
trans conformation is independent of and unrelated to the stereochemistry at the alpha carbon. Therefore, four possible isomers of the compounds disclosed in Bachovshin JBC exist: the *trans*-L,L-isomer, the *trans*-L,D-isomer, the *cis*-L,L-isomer, and the *cis*-L,D-isomer. These four isomers are shown below:



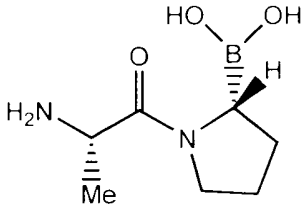
cis-L-Ala-D-boroPro



trans-L-Ala-D-boroPro



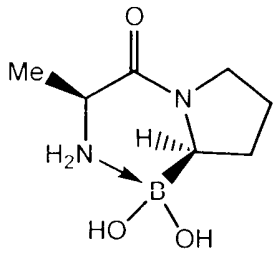
cis-L-Ala-L-boroPro



trans-L-Ala-L-boroPro

As was stated in paragraph 7 of the Declaration filed April 2, 1999, Xaa-boroPro molecules undergo an equilibration between the cis and trans conformation. NMR data supporting this hypothesis was provided in paragraphs 8-12 of the same Declaration and has been published in several scientific papers (Gunther *et al.* "Solution Structures of the DP IV (CD26) Inhibitor Val-boroPro Determined by NMR Spectroscopy" *Magnetic Resonance in Chemistry* 33:959-970, 1995; Sudmeier *et al.* "Solution Structures of Active and Inactive Forms of the DP IV (CD26) Inhibitor Pro-boroPro Determined by NMR Spectroscopy" *Biochemistry* 33:12427-12438, 1994; Snow *et al.* "Studies on Proline Boronic Acid Dipeptide Inhibitors of Dipeptidyl Peptidase IV: Identification of a Cyclic Species Containing a B-N Bond" *J. Am. Chem. Soc.* 116:10860-10869, 1994; Kelly *et al.* "Immunosuppressive Boronic Acid Dipeptides:

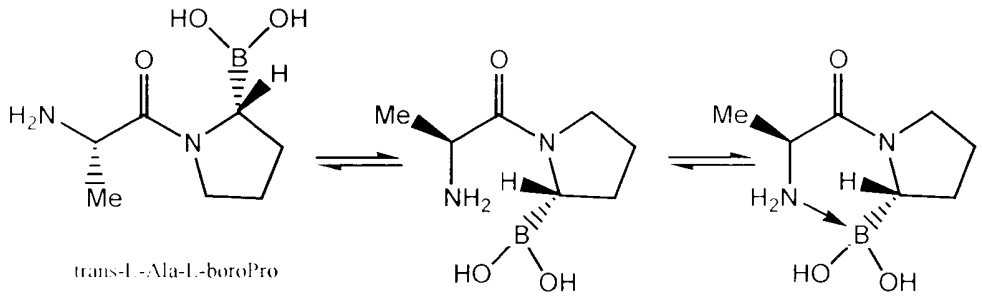
copy of each of these references has been submitted with the IDS for this application and an additional copy has been enclosed herewith). In addition, the *cis* isomer due to the geometry of the boron of proline and the nitrogen of alanine can form a covalent N-->B bond (shown below). The *trans* isomer does not undergo this cyclization (*i.e.*, no N->B bond forms) due to the geometry of the nitrogen and boron (*i.e.*, they are not close enough together in the trans conformation to form a covalent bond), as stated in paragraphs 6 and 12 of the Declaration filed with this Response.



As stated previously in paragraph 13 of the Declaration filed April 2, 1999, the early and later fractions described in Bachovchin JBC do *not* represent the L,L and L,D isomers *but rather the cis and trans isomers*. More specifically, the early fraction represents the trans isomers, both L,L and L,D; and the later fraction represents the cis isomers, both L,L and L,D (see paragraphs 8 and 9 of the Declaration submitted April 2, 1999). The separation effected by silica gel chromatography as described in Bachovchin JBC is based entirely on the cis/trans geometry of the amide bond. There was *no* separation based on the stereochemistry of the alpha-carbon of boroProline; therefore, the L,L and L,D isomers were not separated. The Examiner has proposed separating the L,L and L,D stereoisomers by repeatedly passing the mixture through a silica gel column; however, even multiple passes of the mixture of isomers over a silica gel column would not yield separation of the L,L and L,D isomers (see paragraph 14 of the Declaration submitted with this Response).

One of the reasons given by the Examiner for rejecting the April 1, 1999 Bachovchin Declaration is that "there is a contradiction" in the Declaration because it discusses both a conformation equilibrium and a covalent bond (see Final Office Action of June 24, 1999, page 3, starting on line 1). This statement by the Examiner represents a misunderstanding of the science. There is no contradiction in the Declaration. The "conformation equilibrium on a slow time

of a bond between nitrogen and boron. A molecule in the *cis* conformation may subsequently undergo cyclization with the formation of a nitrogen to boron bond. However, this N->B covalent bond is labile allowing for the N->B bond to break and the *cis* isomer to convert back to the *trans* isomer as shown in the scheme below. As stated above and in paragraph 6 of the Declaration submitted herewith, the *trans* isomer does not form a cyclic structure.



The April 1, 1999 Bachovchin Declaration includes a statement that the results observed in the Bachovchin JBC reference might be explained by co-elution on a silica gel column of the *cis*-L,D and the *cis*-L,L isomers with one another, and the separate co-elution of the trans-L,D and *trans*-L,L isomers. In the June 24, 1999 Final Office Action, the Examiner rejects this conclusion by offering three arguments that are each scientifically flawed.

First, the Examiner offers that the Declaration also asserts the existence of a conformational equilibrium rather than a covalent bond. As discussed above, the conformational equilibrium refers to an equilibrium between the *cis* and *trans* conformations, and is not relevant to the existence of a covalent bond. The fact is that the interconversion of the *cis* and *trans* isomers is on such a slow time scale that the two isomers are separable by silica gel chromatography. There need be no covalent bond in order to effect separation of the two isomers.

Second, the Examiner asserts that "the trans-isomer would not be 'trapped' by the boron atom." This is correct. However, the Examiner goes on to assert that there would be no *cis/trans* isomerization for compounds in which no covalent bonding was present. This is incorrect

formed. *Cis trans isomerization does not rely on the formation of a covalent bond.*

Third, the Examiner questions the identity of the "bone-fide" L,L-isomer, particularly whether it is in the *cis* or *trans* conformation and whether a covalent bond between the boron and nitrogen is present. The NMR spectrum of the "bone-fide" L,L-isomer, presented as exhibit C in the previously filed Declaration, is the spectrum of the trans-L,L-isomer, with no covalent bond present. The Applicant apologizes for not more clearly identifying the structure to which the spectrum pertains and regrets any confusion this may have caused.

Yet another reason given by the Examiner for rejecting the statements of the April 1, 1999 Bachovchin Declaration is that the Examiner simply doubts the existence of a cyclic *trans* isomer (see Final Office Action of June 24, 1999, page 4, line 5-6). The Examiner is correct in that the *trans* isomer does not form a cyclic structure. However, the *cis* isomer does. NMR data provided with the April 1, 1999 Bachovchin Declaration supports the existence of a cyclic *cis* isomer; if those data, in combination with the present Response are insufficient to convince the Examiner of Applicant's position, Applicant respectfully requests that the Examiner provide more specific reasons for challenging the data evidencing existence of the structure.

A final reason given by the Examiner for finding the Bachovchin Declaration and related arguments unpersuasive is that the Examiner asserts that a second pass of the mixture described in the Bachovchin JBC reference through silica gel would provide higher purity, as recited in the present claims (*e.g.*, greater than 95% purity). Once again, this statement reveals the Examiner's misunderstanding of the science. Silica gel chromatography separates *cis* isomers from *trans* isomers, but does not separate L,L isomers from L,D isomers. Thus, no number of passages through silica gel could result in a composition with the claimed isomeric purity.

For all of these reasons, Applicant submits that the Examiner has inappropriately rejected the statements and assertions made in the April 1, 1999 Bachovchin Declaration. That Declaration, in combination with arguments made both in the December 22, 1999 Response to Final Office Action and herein, amply demonstrate that the Bachovchin JBC reference is not enabling; performance of the steps recited in that reference *does not* produce the claimed compositions.

Furthermore, the Examiner's maintenance of the claim rejection over the Bachovchin

the second example presented in the Advisory Action of February 1, 2000. The Examiner states "if chemist published a structure of compound "X", and it turned out that the structure he had determined was not correct, a later chemist would be barred from claiming the published structure for a compound "Y", even if the later chemist were entirely correct in his structure determination." This is not the law. As is clearly stated in **In re Wiggins**, 488 F.2d 538, 179 USPQ 421 (CCPA 1983):

> The mere naming of a compound in a reference, without more, cannot constitute a description of the compound, particularly when, as in this case, the evidence of record suggests that a method suitable for its preparation was not developed until a date later than that of the reference.
>
> If we were to hold otherwise, lists of thousands of theoretically possible compounds could be generated and published which, assuming it would be within the level of skill in the art to make them, would bar a patent to the actual discoverer of a named compound no matter how beneficial to mankind it might be. In view of the fact that the purpose sought to be effectuated by the patent law is the encouragement of innovation, such a result would be repugnant to the statute.

(See also **In re Donohue**, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985)).

The Examiner also apparently misunderstands the facts of the present case. In the Advisory Action of February 1, 2000, the Examiner sets out a "third example" (beginning on page 2 at line 15), which the Examiner characterizes as "closer to the case at hand" than the second example discussed above. The Examiner says "if a first chemist publishes a structure of compound "X", and he later turns out to be absolutely correct, a second chemist would not be granted a patent claim for the structure of compound "X" merely because the first chemist had admitted that he was not absolutely certain of the structure." The issue in the present case is *not* that the authors of Bachovchin JBC were uncertain that they had achieved 95% optical purity, but rather that they did not in fact achieve such purity. Thus, the present situation is closer to Example 2 and not Example 3.

In light of the evidence presented and arguments made herein, Applicant respectfully requests that the rejection over the Bachovchin JBC reference by removed.

This leaves only U.S. Patent 4,935,493 by Bachovchin *et al.*, the publication of the

Sci. USA 88:1556-1559, February 1991). As has already been established, these publications do not teach or suggest a mixture of isomers at least 96% enriched for molecules of the L-configuration at the carbon atom bearing boron, as recited in the present claims. In fact, the Examiner acknowledges that the '493 patent does not form the basis for a proper §102 rejection. And the Examiner has not challenged the assertion by the Applicant that it would not have been obvious to switch from silica gel to a C18 matrix to purify the desired compound. The remaining legal question, then, is whether the disclosure of these references would both (i) motivate a chemist of ordinary skill to try to prepare a composition comprising at least 96% of one isomer; and (ii) provide sufficient guidance for the preparation of such a composition that a chemist would have a reasonable expectation of success. Quite simply, these references do not contain any disclosure that would direct a chemist of ordinary skill to prepare a composition with at least 96% of the carbon atoms bearing boron being of the L-configuration. Moreover, even if the references were to suggest that it might be desirable to prepare such a composition, Applicant has previously pointed out that no method or strategy for obtaining such a composition is provided. The Examiner does not dispute that the '493 patent contains no description of method for preparing an isomerically biased composition. In light of this, these publications cannot render obvious the present claims.

In view of the forgoing arguments, Applicant respectfully submits that the present case is now in condition for allowance. A Notice to that effect is requested.

Please charge any fees that may be required for the processing of this Response, or credit any overpayments, to our Deposit Account No. 03-1721.

Respectfully submitted,

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner For Patents, Washington, D.C. 20231

Choate, Hall & Stewart
Exchange Place
53 State Street
Boston, MA 02109
(617) 248-5000
Date: January 23, 2001

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner For Patents, Washington, D.C. 20231
on January 23, 2001
Karen E Cospo

In re WIGGINS, JAMES, AND GITTOS

(CCPA)
179 USPQ 421

Decided Oct. 11, 1973
No. 8806
U.S. Court of Customs and Patent Appeals

Headnotes

PATENTS

1. Claims — Indefinite — In general (§ 20.551)

If scope of invention sought to be patented is unclear from language of claim, a rejection will lie under second paragraph of 35 U.S.C. 112.

2. Patentability — Anticipation — In general (§ 51.201)

Specification — Sufficiency of disclosure (§ 62.7)

Rejection of compound claims for anticipation under 35 U.S.C. 102(b) does not preclude reliance on additional evidence to show that one of ordinary skill in the art would have known how to prepare claimed compounds at time alleged invention was made; where it might be reasonably doubted that reference or patent application satisfies section 102 or section 112, other references can be cited as evidence of level of skill in the art

3. Patentability — Anticipation — In general (§ 51.201)

Patentability — Invention — In general (§ 51.501)

Naming of compounds by reference does not constitute a description of invention within meaning of

evidence suggests that a method suitable for its preparation was not developed until a date later than that of reference; compounds so named are not "described in a printed publication" as meant by section 102(b); however, naming of compound may be used as evidence of obviousness under section 103 for all it fairly suggests to one of ordinary skill in the art.

4. Patentability — Evidence of — In general (§ 51.451)

In evaluating whether rejection under 35 U.S.C. 103 is proper, evidence not pertinent to a rejection under section 102(b), such as commercial success, unexpected results, etc., may have relevance.

Particular patents—Barbituric Acids

Wiggins, James, and Gittos, Barbituric Acids, claim 2 of application allowed; claims 1 and 10 refused.

Case History and Disposition:

Page 421

Appeal from Board of Appeals of the Patent Office.

Application for patent of Leslie Frederick Wiggins, John William James, and Maurice Ward Gittos, Serial No. 526,707, filed Feb. 11, 1966; Patent Office Group 120. From decision rejecting claims 1, 2, and 10, applicants appeal. Affirmed as to claims 1 and 10; reversed as to claim 2.

Attorneys:

JANES & CHAPMAN (LELAND L. CHAPMAN and JOHN R. JANES of counsel) both of New York, N. Y., for appellants.

S. WM. COCHRAN (JACK E. ARMORE of counsel) for Commissioner of Patents.

Judge:

Before MARKEY, Chief Judge, and RICH, ALMOND, BALDWIN, and LANE, Associate Judges.

Opinion Text

Opinion By:

ALMOND, Senior Judge.

rejection of claims 1, 2, and 10 of appellants' application [1] directed to compounds useful for treating Parkinson's disease. All these claims were rejected under 35 U.S.C. 102(b) and claims 1 and 10 were rejected under 35 U.S.C. 112. We reverse in part and affirm in part.

Invention

Appellants' invention is most broadly set forth in claim 1 reproduced below:

> 1. A compound having anti-Parkinsonism activity selected from the class consisting of compounds of the formula:
> *Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.*
>
> and pharmaceutically acceptable salts thereof, in which formula X is selected from the group consisting of oxygen and sulphur, R_1 is selected from the group consisting of:
> *Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.*
> wherein R_3 represents lower alkyl.

> R_4 represents lower alkyl and A represents a group selected from the class consisting of unsubstituted and methyl-substituted straight-chain alkylene of two to three chain carbon atoms;
> *Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.*
> represents a saturated heterocyclic group of five to seven ring atoms, from one to two nitrogen atoms, and up to one oxygen atom, and A represents a group selected from the class consisting of unsubstituted and methyl-substituted straight-chain alkylene of two to three chain carbon atoms; and
>
> (C) R_5-$(CH_2)_n$-, wherein n is a positive whole number up to 2 and R_5 is a saturated heterocyclic group of five to seven ring atoms, up to one oxygen atom and from one to two nitrogen atoms, said heterocyclic group containing a member selected from the group consisting of unsubstituted and lower-alkyl-substituted basic ring nitrogen atoms spaced away from the adjacent carbonyl groups in the barbituric acid ring by from three to five carbon atoms; and R_2 is selected, when X is oxygen, from the group consisting of:
>
> (D) phenyl, halogenophenyl, hydroxyphenyl, lower alkylphenyl and lower alkoxyphenyl, and when X is sulphur, from the group consisting of:
>
> (E) phenyl, halogenophenyl, hydroxyphenyl, lower alkylphenyl, lower alkoxyphenyl, cyclohexyl, benzyl and straight-chain and branched chain alkyls having from three to seven carbon atoms

[illegible]

When X is oxygen, the compounds embraced by claim 1 are referred to as "oxobarbituric acids." Similarly, when X is sulfur, the compounds are referred to as "thiobarbituric acids." According to appellants' specification, these compounds are useful for the treatment of Parkinson's disease (paralysis agitans), a disease of the nervous system sometimes referred to as "shaking palsy."

The compounds encompassed by the claims can, for the most part, be prepared by a process well known to the prior art involving the condensation of urea or thiourea with a disubstituted malonic ester in the presence of a refluxing solution of sodium in an alcohol (a sodium alcoholate). The disubstituted malonic ester has the formula:
Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

wherein R is a lower alkyl group, preferably ethyl. Appellants term this process a "high temperature condensation."

Appellants found that certain oxo-and thiobarbituric acids could not be prepared this way because the malonic ester required for the synthesis was unstable and decomposed in the refluxing solvent. The malonic esters susceptible to this decomposition are described by appellants as those having the formula:
Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.

wherein R_1 represents:
Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.
wherein R_3 represents a lower alkyl group and A represents an unsubstituted or methyl-substituted straight-chain alkylene radical having 2 or 3 chain carbon atoms; or
Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.
wherein
Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.
represents a heterocyclic group containing from five to seven ring atoms and A represents an unsubstituted or methyl-substituted straight-chain alkylene radical having 2 or 3 chain carbon atoms; or

(C) R_5-$(CH_2)n$-, wherein n is 1 or 2 and R_5 represents 2-pyridyl or N-methyl-2-piperidinyl; and

Z represents hydrogen or at least one halogen, lower alkyl or lower alkoxy substituent, provided that when R represents a dimethylaminoalkyl group which is not substituted by methyl in the alpha position of the alkyl group, Z cannot represent hydrogen, but must be at least one halogen, lower alkyl or lower alkoxy substituent

at this temperature only the thiobarbituric acids could be obtained since urea, unlike thiourea, would not undergo condensation. Therefore, in order to obtain oxobarbituric acids which could not be prepared by the prior art process, appellants added yet another refinement to their process. First, they prepared the thiobarbituric acid analogue of the desired oxobarbituric acid which was then oxidized by a known process to the corresponding oxobarbituric acid. Appellants refer to this process as a "low temperature condensation."

Opinion

Rejection Under § 112

In support of the rejection of claims 1 and 10 under § 112, the examiner, in his "Supplemental Examiner's Answer On Remand," made the following observations:

> The definitions of
> *Graphic material consisting of a chemical formula or diagram set at this point is not available. See text in hard copy or call BNA PLUS at 1-800-452-7773 or 202-452-4323.*
> and "R 5" are indefinite and too broad. The definitions particularly point out the nature of only one, two, or three, of the five to seven ring atoms. The claims are indefinite as to what other ring atoms can be present. The claims are also indefinite as to what and how many substituents the heterocyclic groups can have, if any. The claims are too broad in that there is no proper support for such rings as pyrazolidinyl, isoxazolidinyl, oxadiazolidinyl, etc.—i.e. rings wherein the heteroatoms are not separated by carbon atoms.
>
> Re the rejection as failing to properly define the invention, appellants argue first that "a saturated heterocyclic group of * * * from one to two nitrogen atoms, and up to one oxygen atom" means "a saturated heterocyclic group in which the heteroatoms are all selected from the group consisting of from one to two nitrogen atoms and up to one oxygen atom". Concededly, this is a possible construction of the language, but the language is open to other interpretations. * * * Support for appellants' construction may be found in the fact that the specification discloses only heterocyclic groups containing nitrogen or nitrogen and oxygen.

It would appear that the examiner was of the opinion that appellants were claiming an invention that was broader than any described in their specification (a 1st paragraph, § 112 rejection) and were not distinctly claiming that which they regarded as their invention (a 2nd paragraph, § 112 rejection). The board agreed with the examiner's rejection, commenting, in part, as follows:

> Appellants' arguments do not persuade us of error in the examiner's rejection. The terminology employed is so loose as to be indefinite and to be entirely speculative as to the inclusion of groups forming final products having the therapeutic activity herein required. * * *
>
> It must also be noted that the claim terminology is so broad that it does not even require that the heterocyclic group contain a carbon atom. Heterocyclic ring systems containing

having the properties herein claimed.

[1] In our view, the rejection under § 112 was properly made, at least insofar as it was based on the 2nd paragraph of § 112. That paragraph requires the applicant to "particularly point out and distinctly claim the *subject matter sought to be patented*." In re Borkowski, 57 CCPA 946, 951, 422 F.2d 904, 909, 164 USPQ 642, 645 (1970). If the scope of the invention sought to be patented is unclear from the language of the claim, a second paragraph rejection will properly lie.

In the instant case, the Patent Office questions whether the term "heterocyclic group" as defined in the claims possesses the requisite definiteness. Both the examiner and the board felt the term was not precise enough to allow the scope of the claims involved to be accurately determined. Appellants seek to overcome their specific criticisms by arguing that:

> * * * the claims clearly define the *maximum* breadth, namely, heterocyclic rings containing carbon and nitrogen, or carbon, nitrogen, and oxygen, having from five to seven ring atoms, one or two nitrogen atoms, and up to one oxygen atom. This is a rather limited scope, as heterocyclic rings go. There are many more heterocyclic compounds excluded by the claims than are included by them, such as, for instance, heterocyclic rings containing the two or more oxygen atoms, three or more nitrogen atoms, or one or more sulfur atoms, as well as other types of hetero atoms.

However, we agree with the examiner that appellants' interpretation of the scope of the claim is but one possible construction and that other, broader constructions are possible that are not unreasonable in light of the words of the claims. Words in claims are to be given "their broadest reasonable interpretation consistent with the specification where the patent has not yet issued and the applicant has an opportunity to change them." In re Finsterwalder, 58 CCPA 871, 876, 436 F.2d 1028, 1032, 168 USPQ 530, 534 (1971).

Applying this standard to claims 1 and 10, it is our view that the board was correct when it concluded that the "heterocyclic group" in those claims could be interpreted to include other members than those noted by appellants. Furthermore, the examiner, in his answer, indicated that appellants had support in the specification for a claim of the same scope that appellants would now have us give claims 1 and 10. Therefore, we do not think it would have been difficult to employ language in the claims *precisely* limiting them to that scope.

In view of our affirmance of the rejection under § 112 on the ground that the claims do not satisfy the requirements of the 2nd paragraph, it is not necessary for us to consider whether a rejection made under the 1st paragraph would have been justified.

Rejection Under Section 102(b)

The rejection of claims 1, 2 and 10 under section 102(b) was based upon an article [2] published by Giudicelli et al. (Giudicelli). This reference reports the syntheses of a number of oxobarbituric acid

compounds that do, phenyl-beta-piperidinoethyl barbituric acid and phenyl-beta-morpholinoethyl barbituric acid, whose syntheses were unsuccessfully attempted. The examiner recognized that the failure of Giudicelli to make these compounds was a defect in the reference. Therefore, he cited a second reference, a patent to Donnison, [3] which discloses a process for making oxo- and thiobarbituric acids. This process is similar to appellants' low temperature process.

The examiner concluded that Donnison's process could be used to prepare the compounds named by Giudicelli. The significance of this conclusion can be seen from the legal analysis of that situation, stated by him as follows:

> Giudicelli et al. could not prepare these compounds by their chosen method. However, the test of an "enabling disclosure" is not whether the reference teaches how to make the compounds, but whether the reference taken with the remainder of "the prior art is such as to place the disclosed 'compound' in the possession of the public."

The examiner's authority for this test was the decision of this court in In re Brown, 51 CCPA 1254, 329 F.2d 1006, 141 USPQ 245 (1964). See also In re LeGrice, 49 CCPA 1124, 301 F.2d 929, 133 USPQ 365 (1962); In re Sheppard, 52 CCPA 859, 339 F.2d 238, 144 USPQ 42 (1964); In re Hoeksema, 55 CCPA 1493, 399 F.2d 269, 158 USPQ 596 (1968); In re Collins, 59 CCPA 1170, 462 F.2d 538, 174 USPQ 333 (1972). In his view, Giudicelli is an "enabling disclosure" since Donnison's process could be used to make the named compounds, thereby putting them in the possession of the public. The board agreed.

The examiner's rationale necessarily presumes that Giudicelli both describes the invention and would enable one skilled in the art to make the invention, the former by merely naming the compounds and the latter by viewing Donnison as evidence that one skilled in the art could make the named compounds, thereby making them available to the public.

Appellants argue that the rejection is improper since Giudicelli by itself does not disclose all that is necessary to put the compounds in the hands of the public. Because the Patent Office had to rely upon Donnison to overcome this defect in Giudicelli, appellants insist that the rejection must be considered as having been made over a combination of references. In their view, a rejection based upon a combination of references is proper only if the statutory basis is 35 U.S.C. 103. Alternatively, appellants argue that the process taught by Donnison could not be used to make the named compounds.

The solicitor states the issue as to whether § 102(b) can be the proper statutory basis as follows:

> Does the rejection of compound claims for anticipation under 35 U.S.C. 102(b) preclude reliance on additional evidence to show that one of ordinary skill in the art would have known how to prepare the claimed compounds at the time appellants' alleged invention was made?

[2] The answer to the solicitor's question, and certainly the one desired by him, must be "No." Every patent application and reference relies to some extent upon knowledge of persons skilled in the art to complement that disclosed in order that it be "enabling" within the meaning of § 112 and to satisfy the requirements of a reference under § 102. For example, a reference describing an oil refinery need not describe how to make bolts and rivets in order to be considered "enabling." The hypothetical just stated is

art

[3] However, we do not think that the outcome of this case revolves about the answer to the above-stated question. The defect in the issue, as stated by the solicitor, is that it presumes

that the naming of the compounds by Giudicelli constitutes a description of the invention within the meaning of § 102(b). We do not accept this presumption. In our view Giudicelli's listing of the compounds by name constituted nothing more than speculation about their potential or theoretical existence. The mere naming of a compound in a reference, without more, cannot constitute a description of the compound, particularly when, as in this case, the evidence of record suggests that a method suitable for its preparation was not developed [4] until a date later than that of the reference.

If we were to hold otherwise, lists of thousands of theoretically possible compounds could be generated and published which, assuming it would be within the level of skill in the art to make them, would bar a patent to the actual discoverer of a named compound no matter how beneficial to mankind it might be. In view of the fact that the purpose sought to be effectuated by the patent law is the encouragement of innovation, such a result would be repugnant to the statute. Therefore, we hold that the compounds named in Giudicelli and within the scope of the claims in issue were not "described in a printed publication" as meant by the applicable portion of § 102(b). This dictates a reversal of the rejection of claims 1, 2 and 10 under that section.

Our holding does not mean that a reference merely naming a compound is without effect at all. It may be used as evidence of obviousness under § 103 for all it fairly suggests to one of ordinary skill in the art. In fact, the solicitor suggests in his brief that it wouldn't matter in this case whether we view the statutory basis of the rejection as § 102(b) or § 103. We cannot agree.

[4] In evaluating whether a rejection made under § 103 is proper, evidence not pertinent to a rejection made under § 102(b) may have relevance i.e., commercial success, unexpected results, etc. For example, evidence of commercial success no matter how striking could not overcome a rejection of a claim based on its lack of novelty. It simply is not relevant or material to that point. Therefore, since we do not know what additional evidence appellants might have been able to present if their claims had been rejected under § 103, it would not be proper for us to conjecture whether such a rejection might be sustained.

For the foregoing reasons, the rejection of claims 1 and 10 under 35 U.S.C. 112 is *affirmed*, and the rejection of claims 1, 2 and 10 under 35 U.S.C. 102(b) is *reversed*.

Footnotes

Footnote 1. Serial No. 526,707 filed February 11, 1966.

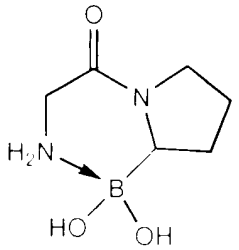
Footnote 2. Annales Pharm. Francaises, Vol. 15, 1957, pp. 533-546.

Footnote 3. U. S. 2,876,225 issued March 3, 1959.

and concluded that it could be used to prepare the claimed compounds. As this is irrelevant to our decision, we express no opinion on this point.

- End of Case -

Rebuttal Evidence to the Rejection of Claims Under 35 USC §103

Asser (Empl	made in Office Action mailed June 24, 1999 added)	Applicant's Rebuttal to Assertion
Asser art arg	1: ". . . Bachovchin has argued that his teachings in this ol. Chem.) were not correct. Specifically, applicant has he following structure is formed:  paragraph 7 of the declaration, there is a contradiction. and, applicant refers to a 'conformation equilibrium on . ne scale'. But on the other hand, the last sentence of states that there is actually a covalent bond that is her there is a covalent bond or there is not."	No contradiction exists. The conformation equilibrium on a slow time scale refers to the conversion of the *trans* to the *cis* conformation of the amide bond. The formation of the covalent bond between the boron and the nitrogen only occurs when the molecule is in the *cis* conformation. This N->B covalent bond is labile allowing for the conversion of the *cis* isomer back to the *trans* isomer. The covalent bond does not form in molecules of the *trans* conformation due to geometric constraints.
Fi Or pa for		
Asser nit pe C L co ho	2: "If there is in fact a covalent bond between the alanyl d the boron that is bonded to the pyrrolidine ring, then ould appear at first blush that the prior results (*J. Biol.*) could be explained by a co-elution (on silica gel) of the the L,L-*cis* isomers with one another, and separately, a f the L,D-*trans* and L,L-*trans* isomers. There are, ree arguments against such a conclusion:	The Examiner's statement concerning the prior results (which has been underlined) *is correct*. There is co-elution of the L,D-*cis* and L,L-*cis* isomers and co-elution of the L,D-*trans* and L,L-*trans* isomers.
co for	nts have stated in paragraph 7, declaration, that there is a nal equilibrium, rather than an outright covalent bond	A conformational equilibrium does exist between the *cis* and *trans* isomer as stated above in paragraph 6. This conformational equilibrium is on a time scale slow enough to allow for the separation of the *cis* and *trans* isomers. In addition, the covalent bond between the boron and nitrogen in the *cis* isomer may contribute to the slowness of the interconversion between the *cis* and *trans* isomers and may

	be what allows one to separate the *cis* and *trans* isomers.
here were covalent bond formation between nitrogen and ins-isomer would not be "trapped" by the boron atom. here would be a mixture of covalently conded "*cis*" structures in which there is no bonding between nitrogen the compounds for which no covalent bonding was e would be no *cis/trans* isomerization.	*Cis/trans* isomerization about the C-N linkage of the amide bond occurs regardless of whether a covalent bond forms. It just so happens that the geometry of the *cis* isomer allows for the formation of a cyclic structure with a B->N bond. Due to the lability of the B->N bond in the *cis* isomer, the molecule is not trapped in the *cis* conformation, but rather the B->N bond may break and the unbonded *cis* isomer may convert back to the *trans* isomer. The geometry of the *trans* isomer does not allow for the formation of such a cyclic structure.
its have provided an NMR spectrum which is asserted to "bona-fide" L,L-isomer. However, in describing the r which this spectrum was obtained, applicants are t about the question of the purported *cis trans* n. The questions remain, for the "bona-fide" L,L-isomer, isomer, of the *trans* isomer, and is there a covalent bond nitrogen of the alanine, and the boron on the pyrrolidine	The term "bone-fide" L,L-isomer, as it refers to the NMR spectrum previously submitted as Exhibit C of the Declaration filed April 2, 1999, represents the isomer in the *trans* conformation. Therefore, the NMR spectrum of the "bone-fide" L,L-isomer presented in the previously filed Declaration is that of the *trans*-L,L-isomer with no B- N bond present.
3: "While it is plausible that there could be some sort of between the nitrogen of the alanine and the boron of the ring, applicants arguments in the declaration are nconvincing. Particularly unlikely is the possibility of a er, given that only a six-membered ring (adjacent to a 5- ng) is being proposed."	The covalent bond between the nitrogen of the alanine residue and the boron of the proline residue only forms when the compound is in the *cis* conformation. The covalent bond does not form in the *trans* conformation due to geometric constraints.
4: "But even if the various contradictions and omissions plained, there would still be one remaining fact, which is sumption of enablement is conferred upon the *J. Biol.* r. If a hypothetical applicant had conducted a series of , and interpreted all of them incorrectly or if a l applicant has conducted no experiments at all, but ers a groundless assertion, that disclosure is considered to ", from a legal perspective, once the patent issues. If the of enablement is granted to someone who has never	Applicant has previously pointed out that the statement made in Bachovchin JBC and relied upon by the Examiner *was an incorrect statement*, as has since been demonstrated in the literature and in declaratory evidence submitted to the Patent and Trademark Office (a copy of the previously submitted Declaration is enclosed with the present Response). The procedures followed in the Bachovchin JBC reference *did not*, and *can not*, produce a composition comprising 95% of one isomer of the compound. Thus, as Applicant has

att en sta	single experiment, then surely the presumption of should be bestowed upon an article in a respected journal ne at issue.	previously argued, the Bachovchin JBC reference does not teach one of ordinary skill in the art to produce a composition comprising 95% of one isomer, does not in fact describe such a composition, and therefore is not an enabling reference against the present claims. As is stated in **In re Wiggins**, 488 F.2d 538, 179 USPQ 421 (CCPA 1983), "the mere naming of a compound in a reference, without more, cannot constitute a description of the compound, particularly when, as in this case, the evidence of record suggests that a method suitable for its preparation was not developed until a date later than that of the reference." As amply described in the Declaration of April 1, 1999 and reiterated and amplified in the Declaration filed with this Response and discussed below, performing steps of Bachovchin JBC *does not* produce the stated result (*i.e.*, a composition containing 95% of one isomer).
Asse Ba stu Ba wh pu p a	**5**: If it is really true that the compound isolated in the *J.* paper was an N->B covalently bonded *trans*-ring at fact is of little import from a legal perspective. , in the *J Biol Chem* paper characterized the compound, was, as the L,L-isomer. Thus, the chemist following the rocedure would readily obtain the compound in 95% a single pass through silica; it is reasonable to expect that ss through silica would provide even higher purity.	Following the procedure in the *J Biol Chem* paper, one would *not* obtain the compound in 95% purity after a single pass through silica. Evidence to this effect was first presented in the previous Declaration filed April 2, 1999. The published procedure provides no separation of the L,L- and the L,D-isomers. A hundred passes through a silica gel column would not result in 95% purity of the desired L,L-isomer.
Asse si ol is co di pa co	**6**: Turning next to the arguments of applicants' attorney, d heavily on the argument that it would not have been switch from silica gel to a C18 matrix. Such an assertion nged, but the extent to which it might be true is of little e with regard to the question of novelty. The claims are mpounds (mixtures), not to a method of separation. The ch the compounds may have been purified is not The reference has described the means to obtain Ala-	Bachovchin JBC does *not* describe the means to obtain AlaboroPro in 95% enantiomeric excess.

bo be sta	95% enantiomeric excess; if the compound has in fact ntified, that is of little consequence from a legal	
As 3 ap wl str wi	7: Applicants have also made reference to *Biochemistry* 993. If applicants wish to rely on this disclosure, re requested to point out the exact location in the text tated that there is a N->B covalently bonded *trans*-ring omments by the examiner with regard to this reference rred pending identification of the relevant passage.	There is no N->B covalently bonded *trans*-ring structure. Only the *cis*-isomer may exist in the N->B covalently bonded cyclic structure.